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REMARKS/ARGUMENTS

Consideration of the captioned application in view of the foregoing amendments and following remarks is requested.

By this Amendment, claims 12, 13, 19 and 20 were canceled. Accordingly, the pending claims are 1-11, and 14-18.

The specification has been amended to refer to the priority applications.

Enclosed herewith is an Information Disclosure Statement with a copy of the International Search Report and documents cited therein.

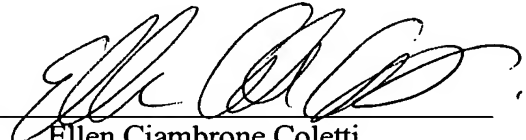
Early favorable action on the merits is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page(s) is/are captioned "Version with markings to show changes made".

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

By: _____



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Dated: February 14, 2002

10075876.021402

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

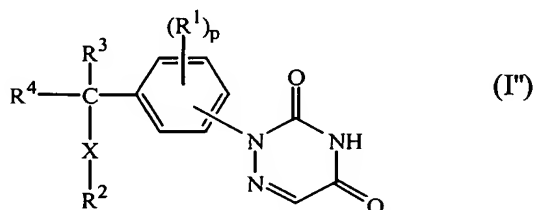
Page 1, between the Title and line 4, please insert the following:

-- Cross Reference to Related Applications

This application is a continuation-in-part application of the national stage application filed February 5, 2002, of Application No. PCT/EP00/07358, filed July 31, 2000 which application claims priority from EP 99870170.0, filed August 6, 1999, and EP 99126035.7, filed December 27, 1999. –

In the Claims:

3. (Amended) A compound according to claim[s] 1 [or 2] having the formula



a *N*-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein :

p represents an integer being 0, 1, 2, 3 or 4;

X represents O, S, NR⁵ or a direct bond or -*X*-R² taken together may represent cyano;

Y represents O, S, NR⁵, or S(O)₂;

each R¹ independently represents C(=O)-Z-R¹⁴, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl, hydroxy, mercapto, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkylcarbonyloxy, aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁₋₄alkyl substituted with C(=O)-Z-R¹⁴, Het³, R⁶ or NR⁷R⁸;

R² represents Het¹, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkyl or C₁₋₆alkyl substituted with one or two substituents selected from C(=O)-Z-R¹⁴, hydroxy,

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cyano, amino, mono- or di(C₁₋₄alkyl)amino, C₁₋₆alkyloxy optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkylsulfonyloxy, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio; and if X is O, S or NR⁵, then R² may also represent aminothiobonyl, C₁₋₄alkylcarbonyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₄alkylthiocarbonyl optionally substituted with C(=O)-Z-R¹⁴, arylcarbonyl, arylthiocarbonyl, Het¹carbonyl or Het¹thiocarbonyl;

R³ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl;

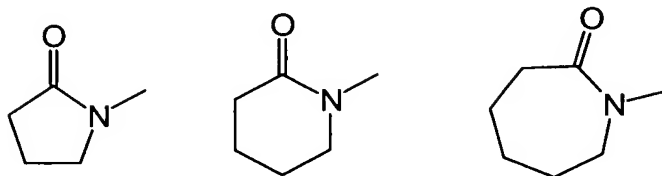
R⁴ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl; or

R³ and R⁴ taken together form a C₂₋₆alkanediyl;

R⁵ represents hydrogen or C₁₋₄alkyl;

each R⁶ independently represents C₁₋₆alkylsulfonyl, aminosulfonyl, piperidynylsulfonyl, mono- or di(C₁₋₄alkyl)aminosulfonyl, mono- or di(benzyl)aminosulfonyl, polyhaloC₁₋₆alkylsulfonyl, C₁₋₆alkylsulfinyl, phenylC₁₋₄alkylsulfonyl, piperazinylsulfonyl, aminopiperidynylsulfonyl, piperidinylaminosulfonyl, N-C₁₋₄alkyl-N-piperidinylaminosulfonyl or mono-or di(C₁₋₄alkyl)aminoC₁₋₄alkylsulfonyl;

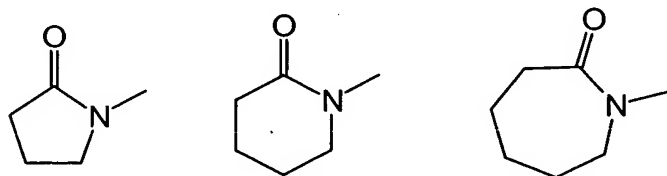
each R⁷ and each R⁸ are independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, aryl, arylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, arylcarbonyl, Het³carbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiobonyl, Het³aminocarbonyl, Het³aminothiobonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and R⁶; or R⁷ and R⁸ taken together with the nitrogen atom to which they are attached form a radical of formula



R⁹ and R¹⁰ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl,

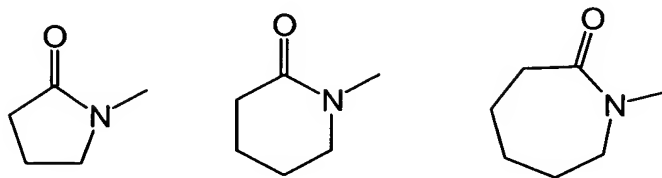
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phenylcarbonyl, Het³carbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, Het³aminocarbonyl, Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and R⁶; or R⁹ and R¹⁰ taken together with the nitrogen atom to which they are attached form a radical of formula



each R¹¹ independently being selected from hydroxy, mercapto, cyano, nitro, halo, trihalomethyl, C₁₋₄alkyloxy optionally substituted with C(=O)-Z-R¹⁴, formyl, trihaloC₁₋₄alkylsulfonyloxy, R⁶, NR⁷R⁸, C(=O)NR¹⁵R¹⁶, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, aryl, aryloxy, arylcarbonyl, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, C₃₋₇cycloalkyloxy optionally substituted with C(=O)-Z-R¹⁴, phthalimide-2-yl, Het³, Het⁴ and C(=O)Het³;

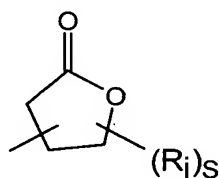
R¹² and R¹³ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, phenylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴ and R⁶; or R¹² and R¹³ taken together with the nitrogen atom to which they are attached form a radical of formula



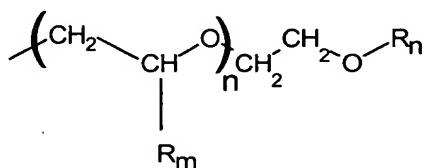
each R¹⁴ independently represents hydrogen, C₁₋₂₀acyl (having a straight or branched, saturated or unsaturated hydrocarbon chain having 1 to 20 carbon atoms), C₁₋₂₀alkyl,

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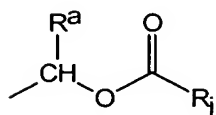
C₃₋₂₀alkenyl optionally substituted with phenyl, C₃₋₂₀alkynyl, C₃₋₇ cycloalkyl, polyhaloC₁₋₂₀alkyl, Het⁵, phenyl or C₁₋₂₀ alkyl substituted with one or more substituents selected from hydroxy, NR¹⁷R¹⁸, phenyl, mono- or di-(C₁₋₄alkyl)amino, cyano, Het⁵, C₁₋₄ alkyloxycarbonyl, phenyl C₁₋₄ alkyloxycarbonyl and C₃₋₇ cycloalkyl, or R¹⁴ represents a radical of formula



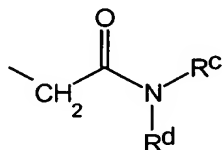
(a)



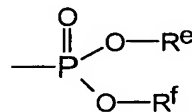
(b)



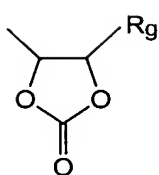
(c)



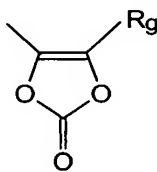
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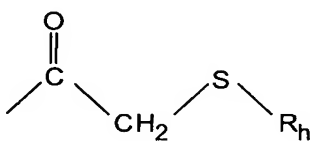
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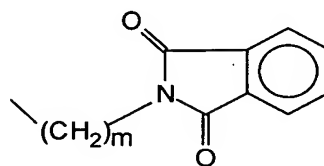
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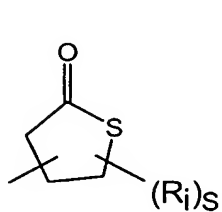
(i)



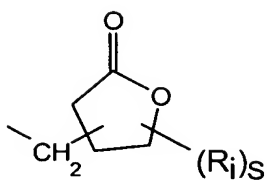
(j)



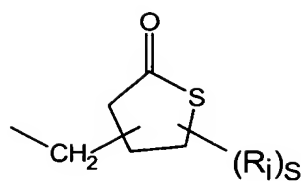
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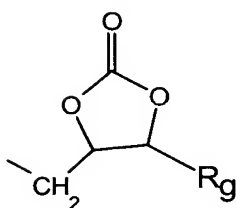
(l)



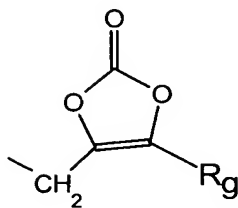
(m)



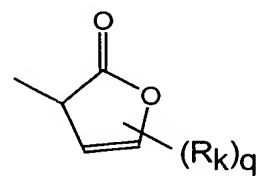
(n)



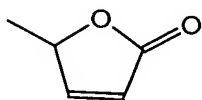
(o)



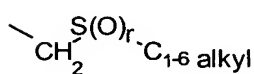
(p)



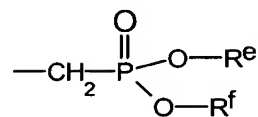
(q)



(r)



(s)



(t)

wherein m is 1 to 4, n is 0 to 5, q is 0 to 2, r is 0 to 2 and s is 0 to 4;

R^a , R^b , R^c , R^d , R^e and R^f are each independently hydrogen, C_{1-6} alkyl, phenyl or C_{3-7} cycloalkyl; or

R^e and R^f taken together may form $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$ or $-CH_2-CH_2-CH_2-CH_2-$;

R_g , R_h and R_k are each independently hydrogen or C_{1-4} alkyl;

R_i is C_{1-4} alkyl;

R_j is $-O-R_b$, C_{1-6} alkyl, phenyl or C_{3-7} cycloalkyl optionally substituted with C_{1-4} alkyloxy;

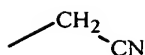
where R_m is hydrogen or C_{1-4} alkyloxy and R_n is hydrogen, C_{1-4} alkyl,

C_{3-7} cycloalkyl, phenyl or phenyl C_{1-4} alkyl

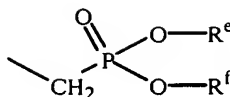
each Z independently represents O, S, NH, $-CH_2-O-$ or $-CH_2-S-$ whereby $-CH_2-$ is attached to the carbonyl group; or

$-Z-R^{14}$ taken together form a radical of formula

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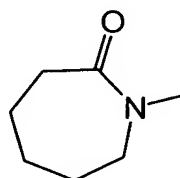
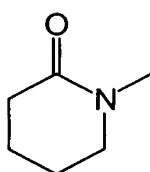
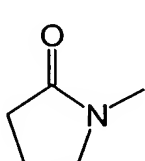


(f)



(g)

R^{15} and R^{16} are each independently selected from hydrogen, C_{1-4} alkyl, hydroxy C_{1-4} alkyl, dihydroxy C_{1-4} alkyl, aryl, aryl C_{1-4} alkyl, C_{1-4} alkyloxy C_{1-4} alkyl, $-C(=O)-Z-R^{14}$, arylcarbonyl, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, arylaminocarbonyl, arylaminothiocarbonyl, aminocarbonylmethylene, mono- or di(C_{1-4} alkyl) aminocarbonylmethylene, Het³amino-carbonyl, Het³aminothiocarbonyl, pyridinyl C_{1-4} alkyl, Het³ or R^6 ; or R^{15} and R^{16} taken together with the nitrogen atom to which they are attached form a radical of formula



R^{17} and R^{18} are each independently selected from hydrogen, C_{1-4} alkyl, hydroxy C_{1-4} alkyl, dihydroxy C_{1-4} alkyl, phenyl, phenyl C_{1-4} alkyl, C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkylcarbonyl, phenylcarbonyl, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, C_{3-7} cycloalkyl, pyridinyl C_{1-4} alkyl, C_{1-4} alkanediyl- $C(=O)-Z-C_{1-6}$ alkyl, $-C(=O)-Z-C_{1-6}$ alkyl, $-Y-C_{1-4}$ alkanediyl- $C(=O)-Z-C_{1-6}$ alkyl and R^6 ;

aryl represents phenyl optionally substituted with one, two or three substituents each

independently selected from nitro, azido, cyano, halo, hydroxy, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} alkyloxy, formyl, polyhalo C_{1-4} alkyl, NR^9R^{10} , $C(=O)NR^9R^{10}$, $C(=O)-Z-R^{14}$, R^6 , $-O-R^6$, phenyl, Het³, $C(=O)Het^3$ and C_{1-4} alkyl substituted with one or more substituents each independently selected from halo, hydroxy, C_{1-4} alkyloxy, $C(=O)-Z-R^{14}$, $-Y-C_{1-4}$ alkanediyl- $C(=O)-Z-R^{14}$, Het³ or NR^9R^{10} ;

Het¹ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl,

pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-*d*]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-*b*]thiazolyl; wherein said heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het², R¹¹ and C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het² and R¹¹;

Het² represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-*d*]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-*b*]thiazolyl; wherein said heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het⁴, R¹¹ and C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het⁴ and R¹¹;

Het³ represents a monocyclic heterocycle selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyranyl; wherein said monocyclic

heterocycles each independently may optionally be substituted with, where possible, one, two, three or four substituents each independently selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹²R¹³, C(=O)-Z-R¹⁴, R⁶ and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, C₁₋₄alkyloxy, phenyl, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, R⁶ and NR¹²R¹³;

Het⁴ represents a monocyclic heterocycle selected from pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and triazinyl;

Het⁵ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyranyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-*d*]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-*b*]thiazolyl; wherein said heterocycles each independently may be substituted with, where possible, one, two, three or four substituents each independently selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹⁷R¹⁸, C(=O)-Z-C₁₋₆alkyl, R⁶, sulfonamido and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, C₁₋₄alkyloxy, phenyl, C(=O)-Z-C₁₋₆alkyl, -Y-C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl, R⁶ and NR¹⁷R¹⁸ ; provided however that

- R² is other than C₁₋₆ alkyloxycarbonylC₁₋₆alkyl or aminocarbonyl; and
- R⁷, R⁸, R⁹ and R¹⁰ are other than aminocarbonyl, C₁₋₄alkylcarbonyloxy-C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonylcarbonyl, C(=O)-O-R¹⁹, C₁₋₄alkanediylC(=O)-O-R¹⁹ or -Y-C₁₋₄alkanediylC(=O)-O-R¹⁹; and
- R¹² and R¹³ are other than C₁₋₄alkylcarbonyloxy-C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl or C₁₋₄alkylcarbonylcarbonyl; and
- R¹¹ is other than C(=O)-O-R¹⁹, Y-C₁₋₄alkanediyl - C(=O)-OR¹⁹, C(=O)NH₂, C(=O)NHC₁₋₄alkyl or C(=O)NHC₃₋₇cycloalkyl; and
- R¹⁵ and R¹⁶ are other than aminocarbonyl, C₁₋₄alkylcarbonyloxy-C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl or C₁₋₄alkyloxycarbonylcarbonyl; and
- aryl is other than phenyl substituted with C(=O)-O-R¹⁹, C(=O)NH₂, C(=O)NHC₁₋₄alkyl, C(=O)NHC₃₋₇cycloalkyl and/or with C₁₋₄alkyl substituted with C(=O)-O-R¹⁹ or Y-C₁₋₄alkanediyl - C(=O)-O-R¹⁴; and
- Het³ is other than a monocyclic heterocycle substituted with C(=O)-O-R¹⁹ and/or with C₁₋₄alkyl substituted with C(=O)-O-R¹⁹ and/or Y-C₁₋₄alkanediyl - (=O)-O-R¹⁹; and

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- in each of the above proviso's R^{19} is defined as hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, aminocarbonylmethylene or mono- or di(C_{1-4} alkyl)aminocarbonylmethylene; and
 - the said compound of formula (I) contains at least one $-C(=O)-Z-R^{14}$ moiety.
4. (Amended) A compound according to [any of] claim[s] 1 [to 3] wherein the 6-azauracil moiety is in the para position relative to the carbon atom bearing the $-X-R^2$, R^3 and R^4 substituents.
5. (Amended) A compound according to [any of] claim[s] 1 [to 4] wherein R^2 is a monocyclic heterocycle selected from pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and triazinyl, wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het^2 , R^{11} and C_{1-4} alkyl optionally substituted with Het^2 or R^{11} .
6. (Amended) A compound according to [any of] claim[s] 1 [to 5] wherein R^3 and R^4 are both methyl and $-X-R^2$ is Het^1 .
7. (Amended) A compound according to [any of] claim[s] 1 [to 6] wherein p is 1 or 2 and each R^1 is chloro.
8. (Amended) A compound according to [any of] claim[s] 1 [to 7] wherein R^3 and R^4 are both methyl, $-X-R^2$ is optionally substituted 2-thiazolyl or 3-oxadiazolyl, the 6-azauracil moiety is in the para position relative to the carbon atom bearing the $-X-R^2$, R^3 and R^4 substituents, and p is 2 whereby both R^1 substituents are chloro positioned ortho relative to the carbon atom bearing the $-X-R^2$, R^3 and R^4 substituents.
11. (Amended) A composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound according to [any of] claim[s] 1 [to 10].

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Please cancel claims 12 and 13.

14. (Amended) [Use of a compound according to any of claims 1 to 10 in the manufacture of a medicament] A method for treating eosinophil-dependent inflammatory diseases comprising administering to a subject in need thereof an effective amount of a compound of claim 1.

17. (Amended) A process of imaging an organ, [characterized by] comprising, administering a sufficient amount of a radiolabelled compound of formula (I) as claimed in claim 1 in an appropriate composition, and detecting the emissions from the radioactive compound.

Please cancel claims 19 and 20.

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